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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,357	PILLARISETTI, SIVARAM	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,17,18 and 20-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 17-18, 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 8/14/06, is acknowledged.

2. Claims 1, 3-5, 17-18, 20-24 are pending and under consideration in the instant application.

3. In view of the amendment filed on 8/14/06, only the following rejections are remained.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 5, 17 and 19 stand rejected under 35 U.S.C. 102(b) as being anticipated by Paka *et al* (abstract Nov. 2, 1999) for the same reasons set forth in the previous Office Action mailed 3/10/06.

Applicant's arguments, filed 8/14/06, have been fully considered, but have not been found convincing.

Applicant argues that the Paka et al reference differs from the reference teachings only by the recitation that the HSPG is perlecan or syndecan in claims 3-4 and 22-23. Further Applicant argues that the claimed invention differs from the reference teachings only by the recitation that the HSPG is glygican in claims 3 and 24. Yet, the PTO maintains the rejection under 102(b).

However, claims 3-4 and 22-24 are not included in the 102(b) rejections, Accordingly, Applicant argument is irrelevant to claims 1, 5, 17 and 19, which are rejected under 102(b) as being anticipated by Paka et al abstract.

Applicant argues that the Paka abstract measures the (^{3}H)thymidine incorporation, while the rejected claims recite measuring HSPG to determine the affect of a compound on proliferation. Applicant submits that the reference abstract measure proliferation and HSPG, HSPG are not measured to determine the affect of apoE on proliferation per se.

Contrary to Applicant assertions, Paka et al abstract measured ^{35}SO4 incorporation into media (measuring total PGs in the media) and measured perlecan mRNA expression (a species of HSPG) to determine the affect of apoE on proliferation. Applicant admits on page 7 of the response dated 8/14/06 that one of ordinary skill in the art would recognize that measuring mRNA in the cell culture includes measuring mRNA in cells. Therefore, Paka et al determine the affect of apoE on proliferation by measuring perlecan mRNA in the cell culture.

6. Claims 1, 3-5, 17, 19-20 and 22-23 stand rejected under 35 U.S.C. 102(b) as being anticipated by Paka *et al* (JBC, Dec. 1999, IDS Ref. No. 22) for the same reasons set forth in the previous Office Action mailed 3/10/06.

Applicant's arguments, filed 8/14/06, have been fully considered, but have not been found convincing.

Applicant submits that despite the asserted differences between Paka et al reference and the claimed invention, the PTO maintains its rejection under 102(b). In particular Applicant points Office Action states that the claimed invention differs from the reference teachings only by recitation of compound comprising unknown cellular proliferation activity in claims 1, and 22-24, and that the HSPG is glypican in claims 3 and 24.

Contrary to Applicant submission, the Paka et al reference anticipates the claimed invention. Paka *et al* teaches the effects of ApoE isoforms (E2, E3 and E4) and anti-perlecan antibody (compounds comprising unknown cellular proliferative activity) on perlecan production and proliferation (see Fig. 6 and 7). Claim 3 is limited to glypican but claims also perlecan. Claim 24 was not included in the rejection under 102(b). Accordingly Applicant argument is irrelevant to the anticipatory rejection by Paka et al (JBC reference).

Applicant submits and in contrary to the PTOs assertion, that Paka measures and compares the amount of HSPG to indicate HSPG levels. Applicant submits that Paka reference measures (^{3}H)thymidine incorporation, while the rejected claims recite measuring HSPG to determine the affect of a compound on proliferation. Applicant contends that even though Paka reference measure proliferation and HSPG, HSPG are not measure to determine the affect apoE on proliferation per se.

Contrary to Applicant assertions, Paka reference teaches that PGs are isolated from SMC medium and purified by DEAE-cellulose chromatograph. Pruified PGs are immunoprecipitated with an anti-perlecan antibody, and analyzed by 5% SDS-PAGE to study the effects of ApoE isoforms (E2, E3 and E4) and anti-perlecan antibody on perlecan production and proliferation in addition to measuring thymidine incorporation (to measure cell proliferation).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 3-5, 17 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paka *et al* (Dec, 1999) in view of Lee (2000) for the same reasons set forth in the previous Office Action mailed 3/10/06.

Applicant's arguments, filed 8/14/06, have been fully considered, but have not been found convincing.

Applicant argues that neither paka nor Lee, individually or when combined, teach Applicant's claimed invention comprising determining proliferation by measuring HSPG. In particular, Applicant contends that Paka (JBC) determines proliferation by measuring incorporation of radioactivity whereas lee proposes determining proliferation by counting cells.

Contrary to Applicant assertions, Paka reference teaches that PGs are isolated from SMC medium and purified by DEAE-cellulose chromatograph. Pruified PGs are immunoprecipitated with an anti-perlecan antibody, and analyzed by 5% SDS-PAGE to study the effects of ApoE isoforms (E2, E3 and E4) and anti-perlecan antibody on perlecan production and proliferation in addition to measuring thymidine incorporation (to measure cell proliferation). Therefore, the combined reference teachings arrived to the claimed invention.

Applicant submits that there is a lack of any suggestion or motivation, either in the reference themselves or in the knowledge generally available to one of ordinary skill in the art, to combine or modify reference teachings. Further, Applicant submits that Paka (JBC) reference appears to teach away from such a modification.

Contrary to Applicant assertions, Lee indicates the desire to identify compounds that may be more potent than HSPG in inhibiting restenosis, or co-administration of these compounds with heparin may prove an effective therapy.

In contrast to applicant's assertions of teaching away by the prior art because the references indicate a successful method of for detecting a compound that affects cell proliferation by measuring the amount of a HSPG in the cell culture; there is no discouragement nor skepticism in the prior art for identifying a compound comprising unknown cellular proliferation activity, particularly in light of the prior art desire to identify compounds that may be more potent than HSPG in inhibiting restenosis.

9. Claims 1, 3 and 24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Paka *et al* (Dec. 1999) in view of Lee (2000) and U.S. Pat. No. 6,306,613 for the same reasons set forth in the previous Office Action mailed 3/10/06.

Applicant's arguments, filed 8/14/06, have been fully considered, but have not been found convincing.

Applicant argues that neither Paka (JBC) Lee nor the `613 patent, individually or in combination, teach Applicant's assay method for detecting a compound that affects proliferation by measuring HSPG. Paka et al. (JBC) determines proliferation by measuring incorporation of radioactivity. Lee (2000) proposes determining proliferation by counting cells. And, the '613 patent mentions determining proliferation by using incorporation of tritiated thymidine

Again, Paka reference teaches that PGs are isolated from SMC medium and purified by DEAE-cellulose chromatograph. Pruified PGs are immunoprecipitated with an anti-perlecan antibody, and analyzed by 5% SDS-PAGE to study the effects of ApoE isoforms (E2, E3 and E4) and anti-perlecan antibody on perlecan production and proliferation in addition to measuring thymidine incorporation (to measure cell proliferation). Therefore, the combined reference teachings arrived to the claimed invention.

10. Claims 1, 3-4 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paka *et al* (abstract Nov. 2, 1999) in view of Paka *et al* (JBC, Dec. 1999, IDS Ref. No. 22) for the same reasons set forth in the previous Office Action mailed 3/10/06.

Applicant's arguments, filed 8/14/06, have been fully considered, but have not been found convincing.

Applicant submits the same discussions under 102 rejections above. Further, Applicant submits that neither of the references teaches Applicant's determining proliferation by measuring HSPG. But both references determine proliferation by measuring incorporation of radioactivity or by counting cells.

However, Applicant admits on page 7 of the response dated 8/14/06 that one of ordinary skill in the art would recognize that measuring mRNA in the cell culture includes measuring mRNA in cells. Paka et al (abstract) teaches the ability of apoE isoforms to inhibit SMC proliferation correlated with their ability to stimulate perlecan production and E2 and E4 were less effective in stimulating perlecan. Paka abstract further teaches that analysis of the conditioned medium from apoE stimulated cells revealed that the HSPG increase was perlecan and apoE also stimulated perlecan mRNA expression to be stimulated by > 2folds. Therefore, Paka et al determine the affect of apoE on proliferation by measuring perlecan mRNA in the cell culture and measuring total HSPG (^{35}SO4) in the media.

Further, Paka (JBC) reference teaches that PGs are isolated from SMC medium and purified by DEAE-cellulose chromatograph. Purified PGs are immunoprecipitated with an anti-perlecan antibody, and analyzed by 5% SDS-PAGE to study the effects of ApoE isoforms (E2, E3 and E4) and anti-perlecan antibody on perlecan production and proliferation in addition to measuring

thymidine incorporation (to measure cell proliferation). Therefore, the combined reference teachings arrived to the claimed invention.

11. Claims 1, 3 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paka *et al* (abstract Nov. 2, 1999) or Paka et al (Dec. 1999, IDS Ref. No. 22) in view of U.S. Pat. No. 6,306,613for the same reasons set forth in the previous Office Action mailed 3/10/06.

Applicant's arguments, filed 8/14/06, have been fully considered, but have not been found convincing.

Applicant submits that nowhere does the `613 patent either disclose or suggest the use of HSPG, or specifically a glypican, in a method for detecting a compound that affects cell proliferation where proliferation is determined by measuring HSPG. Applicant disagrees with the PTO's assertion that the `613 patent teaches that "glypican plays a role in regulating cellular proliferation". Applicant contends that just because the `613 patent may mention that glypican is part of a growing family of cell surface HSPGs that play a role in regulating cellular proliferation, it does not follow that the statement teaches or suggests that glypican has a role in regulating proliferation. Further, Applicant submits that neither Paka abstract nor Paka's JBC reference nor the `613 patent, individually or when combined, teach the Applicant's assay method for detecting a compound that affects proliferation by measuring HSPG. Applicant contends that both Paka abstract and JBC paper determine proliferation by measureing incorporation of radioactivity or by counting cells. Further, the `613 patent proposes determining proliferation, if at all, by using incorporation of tritated thymidine.

The Examiner is confused with respect to Applicant's comments about the `613 patent teachings that K-glypican is part of a growing family of cell surface heparin sulfate proteoglycans (HSPGs) that play a role in regulating cellular proliferation. It is not clear to the Examiner as to why the this teaches does not suggest/teach that glypican has role in regulating proliferation.

again, Applicant admits on page 7 of the response dated 8/14/06 that one of ordinary skill in the art would recognize that measuring mRNA in the cell culture includes measuring mRNA in cells. Paka et al (abstract) teaches the ability of apoE isoforms to inhibit SMC proliferation correlated with their ability to stimulate perlecan production and E2 and E4 were less effective in stimulating perlecan. Paka abstract further teaches that analysis of the conditioned medium from apoE stimulated cells revealed that the HSPG increase was perlecan and apoE also stimulated perlecan mRNA expression to be stimulated by > 2folds. Therefore, Paka et al determine the affect of apoE on proliferation by measuring perlecan mRNA in the cell culture and measuring total HSPG (^{35}SO4) in the media.

Further, Paka (JBC) reference teaches that PGs are isolated from SMC medium and purified by DEAE-cellulose chromatograph. Purified PGs are immunoprecipitated with an anti-perlecan antibody, and analyzed by 5% SDS-PAGE to study the effects of ApoE isoforms (E2, E3 and E4) and anti-perlecan antibody on perlecan production and proliferation in addition to measuring

thymidine incorporation (to measure cell proliferation). Therefore, the combined reference teachings arrived to the claimed invention.

Therefore, the combined reference teachings arrive to the claimed invention by measure the amount of glypican as taught by the `613 patent in determining cell proliferation method as taught by Paka et al references. It is noted that the claims do not specify a specific assay of measuring the amount of glypican.

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

October 13, 2006

Maher Haddad

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